Chapter 1

Introduction to the Nutritional Management of Oncology Patients

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INTRODUCTION

Although the precise number of new cases of cancer that occur each year is unknown, the incidence in the United States was greater than 1.4 million cases in 2007.[1] This number does not include diagnoses of carcinoma in situ (with the exception of urinary cancer), nor does it include basal and squamous cell cancers of the skin.[2] Cancer is the cause of death in approximately 23% of deaths each year in the United States[2] and is currently estimated to be the leading cause of mortality for American adults younger than the age of 85. The current lifetime risk for Americans is estimated as one in three among women and one in two among men.[2] Table 1.1 shows the estimated number of deaths by cancer site and by gender in the United States in 2008.

The lifetime probability of developing cancer is greater for men (46%) than for women (38%), although many young women are diagnosed with breast cancer, thereby placing women at a higher risk of developing cancer before the age of 60.[1] While cancer rates differ greatly throughout the world, rates are projected to more than double by the year 2030.[3] Projected increases are due to several factors:

- Growth of the worldwide population
- Aging of the population
- Improved screening, detection, and treatments, resulting in higher survival rates
- Projected increases in tobacco use
- Increases in the number of individuals with HIV/AIDS in some countries[3]

Table 1.1 *Estimated Cancer Deaths in the United States, 2008*

Men		*Women*	
Lung and bronchus	31%	Lung and bronchus	26%
Prostate	10%	Breast	15%
Colon and rectum	8%	Colon and rectum	9%
Pancreas	6%	Pancreas	6%
Liver, intrahepatic, and bile ducts	4%	Ovary	6%
Leukemia	4%	Non-Hodgkin's lymphoma	3%
Esophagus	4%	Leukemia	3%
Urinary bladder	3%	Uterine corpus	3%
Non-Hodgkin's lymphoma	3%	Liver, intrahepatic, and bile ducts	2%
Kidney and renal	3%	Brain/other nervous system	2%
All other sites	24%	All other sites	25%

Source: Data from American Cancer Society, www.cancer.org.

Worldwide, the most commonly diagnosed cancers (excluding skin cancers) are lung, breast, and colorectal cancers, with lung cancer being the primary cancer cause of death.[3] In developed countries, hormonal-related cancers are the most prevalent types of cancer; in underdeveloped areas, the most common cancers are those arising from infectious agents. In men, prostate cancer is the most common type of cancer in high-income countries, followed by lung, stomach, and colorectal cancers. In men in underdeveloped countries, lung cancer prevalence exceeds esophageal, stomach, and liver cancer prevalence. In women residing in developed countries, breast cancer is the most commonly diagnosed cancer, followed by lung, colorectal, and endometrial cancers. In underdeveloped countries, breast cancer is also the most prevalent cancer diagnosed in women, followed by lung, stomach, and cervical cancers.[3]

This chapter provides an overview of how cancer and oncological therapies affect individuals' nutritional status. A brief introduction to nutrition intervention is also given.

Cancer Development

Cancer is actually a cluster of more than 100 diseases that arise due to uncontrolled cellular growth. Normal cellular growth and differentiation are

controlled by a myriad of complex systems, which involve a number of physiologic functions such as cell signaling and gene expression that influence cellular development and communication, as well as cell death. The development of cancer is a multistep process that occurs in three stages: initiation, promotion, and progression.

Initiation is the first step in the development of precancerous cells. In this stage, the cell has been exposed to stress, such as oxidative stress, or to endogenous or exogenous carcinogens; precancerous cells form when the cell undergoes such exposure and either fails to repair itself or fails to die. Subsequently, the cell forms DNA adducts (intermediates formed during phase I metabolism in the liver that may be carcinogenic and bind to DNA), which in turn distort the DNA, disrupting its replication and possibly its translation.[3] Carcinogenic activation can occur through the interaction between dietary and/or environmental components and the enzymes involved in the detoxification phase of metabolism, where phase II enzymes are responsible for producing by-products that can be excreted in the bile or urine. Any of the enzymes that participate in phase I and II metabolism represent potential targets for carcinogenesis, which can be either promoted or prevented during the initiation phase. Initiation alone is not enough for a cell to become cancerous; the cell must then go through the promotion stage. However, the more precancerous cells that are initiated, the greater the risk for developing cancer.

During stage 2, the initiated cancer cell is further stimulated through cell signaling, which allows for cellular replication and growth leading to excess DNA damage that is beyond the capacity of the cell to repair the damage. This process, called cellular proliferation or promotion, is critical in the carcinogenesis process. As the expression of cellular receptors for growth factors increases, intracellular exposure of such growth factors also increases, such that division and growth of the abnormal cell are perpetuated. Further damage to the cell results in alterations in gene expression and cellular proliferation. Clusters of abnormal cells develop, subsequently resulting in tumor formation. Consequently tumor types can be characterized by specific genetic lesions that develop during each step of the carcinogenesis pathway. Nevertheless, there may be significant individual variability in the sequence of genetic lesions or in the quantity of clusters "required" to develop a tumor.

During the promotion stage, precancerous lesions (versus precancerous cells associated with initiation) can usually be detected, although the degree to which a given precancerous lesion evolves into a cancer is not always known. In the final stage, known as progression, the cluster of abnormal cells (i.e., the tumor) may grow into a larger lesion and/or translocate into other areas of the body, resulting in metastasis of cancer cells to other parts of the body.

An understanding of cancer biology is important to understand the impact of diet and other lifestyle components on cancer. An in-depth discussion of this topic is beyond the scope of this chapter, however.

Causes of Cancer

A number of exogenous factors are known to cause cancer, including the following:[3]

- Tobacco use
- Infectious agents (e.g., bacteria, parasites, viruses)
- Medications
- Radiation
- Chemical exposure (e.g., polychlorinated biphenyls, organic compounds used in plastics, paints, adhesives)
- Carcinogenic components found in foods and beverages (e.g., aflatoxins, heterocyclic amines, polycyclic aromatics hydrocarbons, N-nitroso compounds)

Endogenous causes of cancer include inherited germ-line mutations, oxidative stress, inflammation, and hormones. Most cancer experts believe that the majority of cancers are not inherited, but rather arise from alterations in gene expression that promote changes in DNA; over many years, these mutations develop into cancerous tumors. Many nutrients have been shown to influence cell-cycle progression and proliferation.[3] For example, vitamin A can result in cell-cycle arrest. Likewise, retinoids can inhibit cellular proliferation of initiated cells by inducing apoptosis or inducing differentiation of abnormal cells back to normal.[4] Conversely, heme iron has been found to promote cellular proliferation of colonocytes.[5]

Because both exogenous and endogenous factors promote the initiation and progression of cancer, it is often difficult to determine the precise etiology of specific cancers. Many of these factors interact with one another, as modifiers or precursors, potentially resulting in either an increase or a decrease in cancer risk.

In addition to single nutrients' effects on cellular functions, energy intake and physical activity have been noted to alter pathophysiology. In animal studies, energy restriction has been found to prevent cancer to a significant extent.[6, 7] Suppression of tumor development in mice and an increase in lifespan in rodents have been observed with energy restriction.[6] Energy restriction results in reduced circulating levels of insulin-like growth factor 1 (IGF-1) and insulin, both of which serve as growth factors for many cancer

cells. Other inflammatory markers also decline with energy restriction. To date, these observations have not been confirmed in human studies, and further research is needed to explore the specific mechanistic effects in humans. Physical activity (PA) has been found to improve insulin sensitivity and reduce insulin levels.[8] Additionally, PA decreases serum estrogen and androgen levels in both premenopausal and postmenopausal women, thereby potentially providing a protective effect against hormone-related cancers.

Lifestyle Factors

Historically, as populations have evolved from a primarily agricultural society to an urbanized culture, the quality of foods and beverages consumed has changed rapidly—as have their impact on the risk for disease. Since the second half of the twentieth century, more and more evidence has accrued showing that diet plays a significant role in the development of many of the primary causes of death in the United States, including heart disease, some types of cancers, diabetes, stroke, and kidney disease. Although cessation of tobacco use is the most critical modifiable risk factor in preventing cancer, body weight, diet, and PA are thought to play prominent roles in both the primary and tertiary prevention of breast, colorectal, ovarian, endometrial, and prostate cancers.[3]

Paralleling the change in dietary habits that tends to accompany economic development and urbanization, profound changes in PA patterns have also occurred with industrialization: Populations have become extremely sedentary as urbanization and technologic advancements have been integrated into societies. PA is thought to play a key role in the development of chronic disease and some types of cancers. Strong evidence suggests that increased levels of PA reduce the risk for colorectal and breast cancers.[9] Evidence is also accruing that regular PA is beneficial for reducing risk for cancer in cancer survivors.[10–13]

These subsequent lifestyle changes have resulted in another problem that is becoming a global epidemic—namely, obesity. Since the 1980s, the number of people worldwide who have become overweight or obese has skyrocketed. In the United States, more than 66% of the population is considered overweight or obese. In the United Kingdom, 65% of men and 56% of women are overweight, and 22% of men and 23% of women are obese. In China, more than 20% of the population is considered overweight in some cities, while the number of people considered obese has increased to 7% of the population. Although the latter rate is considered low in comparison to the obesity rates observed in other countries, it represents a tripling in obesity from 1992 to 2006.[3] Obesity is projected to continue increasing within the worldwide population.

Body Composition

In addition to diet and PA, the supporting evidence that the presence of excess body fat increases the risk for developing certain types of cancers is convincing.[3] As previously described, the number of overweight and obese individuals worldwide is increasing at an alarming rate. Excess body weight—and particularly excess body fat—increases the risk not only for certain cancers, but also for heart disease, stroke, type II diabetes, hypertension, and many other medical conditions. Given the prevalence of overweight and obesity, both conditions are likely to have a significant impact on the incidence of obesity-related cancers in years to come as the number of individuals with excess body weight and fat continues to increase.

In their recent systemic review of the literature, Renehan and colleagues[14] found that a higher body mass index (BMI) is associated with an increased risk for the following cancers: thyroid, renal, colon, adenocarcinoma of the esophagus, multiple myeloma, leukemia, and non-Hodgkin's lymphoma. Rectal and malignant melanoma cancers are increased in men with a higher BMI, while incidence of cancers of the gallbladder, pancreas, endometrium, and breast (postmenopausal women) is greater in women with a higher BMI. Obesity is also associated with a poorer prognosis in cases of breast, colon, prostate, endometrial, and ovarian cancers.[14]

Although the precise mechanisms of how excess body weight increases the risk for cancer are poorly understood, potential mechanisms that have been cited include changes in circulating endogenous hormones such as insulin, insulin-like growth factors, and sex steroids, as well as changes in the metabolism of adipokines, localized inflammation, oxidative stress, altered immune response, hypertension, and lipid peroxidation.[14] Much speculation surrounds the insulin–cancer hypothesis in particular: Chronic hyperinsulinemia is known to reduce circulating levels of insulin-like growth hormone (IGF) binding protein 1 and IGF-binding protein 2, thereby increasing the availability of IGF, which in turn promotes an environment that favors tumor formation. Adiponectin, which is primarily secreted by adipocytes, is the most abundant circulating adipokine. Its secretion is inversely correlated with BMI; women typically have greater concentrations of adiponectin than men. The benefits of greater adiponectin concentrations lie in its anti-inflammatory, antioxidant, antiangiogenic, and insulin-sensitizing properties. Although some studies have noted inverse correlations between cancer risk and adiponectin levels,[15, 16] further research is needed to delineate this relationship given the early stages of these observations.

Cancer and Nutritional Status

The continuum of cancer survival includes treatment and recovery as well as living with advanced cancer. Each stage is associated with different needs and challenges for the patient, caregivers, and clinicians. Both cancer and the oncological therapies utilized for its treatment can have profound effects on an individual's nutritional status, thereby making nutrition an important component of medical care. Malnutrition is characterized by a variety of clinical symptoms, including weight loss, poor wound healing, electrolyte and fluid imbalances, depressed immune function, and increased morbidity and mortality.

Although all patients with cancer are at nutritional risk, not all patients with cancer become malnourished. Therefore, nutrition screening and the nutrition care process—including nutrition assessment, ongoing monitoring, and follow-up—are crucial for preventing or minimizing the development of malnutrition at all stages of treatment. This plan of care allows for the implementation of the appropriate intervention to target problem areas as warranted. Long-term follow-up upon completion of therapy is also recommended, as nutrition-impact symptoms may be experienced even as long as 12 months following commencement of therapy and have been associated with reductions in quality of life.[17]

Cancer and Malnutrition

One of the most significant nutritional issues that can arise during cancer treatment is malnutrition. Malnutrition may result from the disease process, from the use of antineoplastic therapy, or from both. Side effects related to common oncological therapies, including chemotherapy, radiation, immunotherapy, and surgery, are key contributors in promoting a deterioration in nutritional status. Additionally, deteriorations in nutritional status have been found to predict outcome prior to the initiation of therapy. Dewys and colleagues found that as little as a 6% weight loss predicted response to therapy.[18] These researchers also noted that overall survival rates, performance status, productivity, and quality of life declined concurrently with weight loss in cancer patients. Of note, approximately 80% of the study patients presented with weight loss before being diagnosed with cancer.

Malnutrition also has a detrimental effect on quality of life. Patients with cancer cachexia reported that alterations in body image negatively affected their self-esteem, relationships, spirituality, physical activity, and social functioning.[19]

Cancer Cachexia

Cancer cachexia is a multifactorial syndrome that encompasses a spectrum ranging from early weight loss to significant deteriorations in body fat and lean muscle tissue resulting in death. The term "cachexia" is derived from the Greek words *kakos*, meaning "bad," and *hexis*, meaning "condition."[19] Although no precise definition has been established for cancer cachexia, also known as cancer anorexia–cachexia syndrome (CACS), cachexia is manifested by weight loss and loss of lean body mass. The wasting exhibited by people with cancer and some other conditions (such as cardiac cachexia and chronic obstructive pulmonary disease) is significantly different from that seen in patients with simple starvation: The former individuals experience profound weight loss and loss of lean tissue mass, whereas in persons with starvation lean body mass is generally preserved until the late stages of starvation. Reportedly, 50% of patients with cancer lose some body weight, with one third losing more than 5% of their original body weight and as many as 20% of cancer deaths resulting from cachexia.[20, 21]

Reductions in oral intake alone do not explain why malnutrition often occurs in people with cancer; indeed, cachexia may occur in patients who consume apparently sufficient calories.[20] Moreover, nutrition support does not successfully restore the loss of lean body mass with CACS.

Mediators of Malnutrition

Although the mechanisms leading to cachexia arise from complex tumor–host interactions, a number of metabolic abnormalities that result in catabolism rather than anabolism have been identified. Known factors contributing to the development of CACS include anorexia, early satiety, taste changes, nausea, diarrhea/constipation, fatigue, and anemia. Cachexia also results from an imbalance between pro-inflammatory and anti-inflammatory cytokines. Pro-inflammatory cytokines, including tumor necrosis factor (TNF), interleukins 1 and 6 (IL-1 and IL-6), and interferon gamma (IFN-γ), are thought to be the primary mediators associated with the development of CACS.[22] Cytokines are glycoproteins and cell signaling proteins secreted by a wide variety of hematopoietic and non-hematopoietic cell types (e.g., macrophages, monocytes, lymphocytes, and endothelial and epithelial cells) in response to malignancy, injury, or infection. These cytokines are thought to work in concert, rather than individually, in promoting catabolism and malnutrition.

Figure 1.1 illustrates the array of factors contributing to the development of malnutrition and cachexia. The infusion of pro-inflammatory cytokines in animal studies was found to produce anorexia, weight loss, proteolysis and

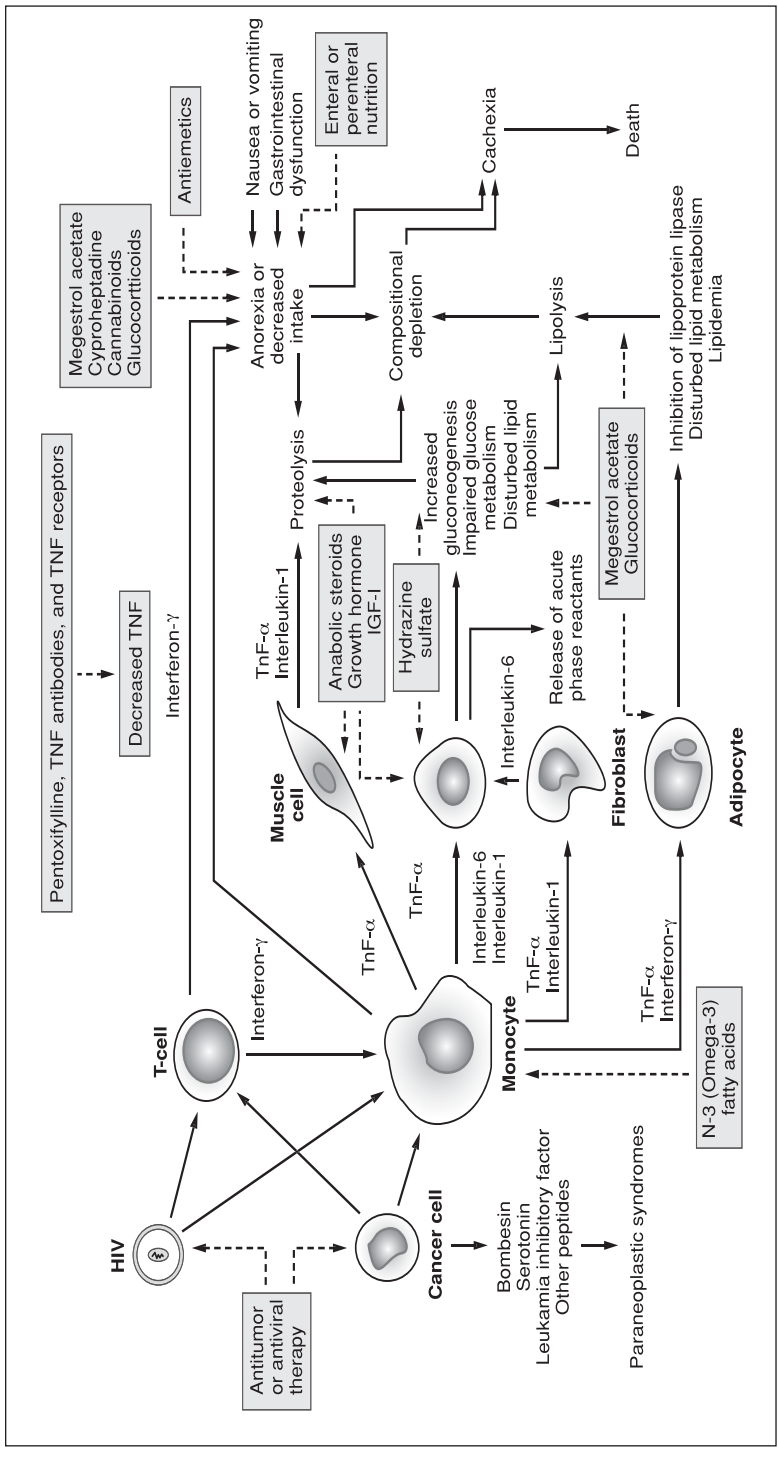

Figure 1.1 *Proposed and Known Mediators That Promote the Complex Tumor-Host Interactions Resulting in Cancer Cachexia*
Adapted from Tchekmedyian NS. Clinical approaches to nutritional support in cancer. *Curr Opin Oncol.* 1993;5(4):633-638.

lipolysis, and elevations in cortisol and glucagon levels in addition to increasing energy expenditure.[23]

Leptin and ghrelin are two hormones that influence appetite and oral intake. Ghrelin increases appetite, whereas leptin reduces appetite. In cancer patients, increases in ghrelin levels and reductions in leptin levels have not resulted in increases in oral intake.[24] Downregulation of leptin production and expression of leptin receptors in the hypothalamus by tumor necrosis factor have been reported, however.[24] Reductions in gastric production of ghrelin synthesis by various cytokines have also been noted. While the relationship between the cytokines, leptin, and ghrelin in regard to CACS requires further investigation, alterations in neurohormonal balance are hypothesized to contribute to CACS.[24]

Another mediator thought to play a role in the development of cancer cachexia is proteolysis-inducing factor (PIF), a glycoprotein that has been isolated from the urine of weight-losing cancer patients. Interestingly, PIF has not been found in persons losing weight from other causes.[25] Additionally, several neurotransmitter systems within the hypothalamus are thought to contribute to the development of CACS. For example, increases in serotonin result in the activation of melanocortin neurons, which are thought to cause anorexia, although their precise role requires further study.[24]

Changes in energy, carbohydrate, protein, and lipid metabolism have also been cited as causes of weight loss in patients with cancer. Alterations in carbohydrate metabolism have been noted in patients with CACS, including both glucose intolerance and insulin resistance, although this effect varies with the type of cancer.[26] Glucose intolerance has been noted to increase with increases in tumor burden, leading to increasing insulin resistance and weight loss.[26] Increases in glucose utilization combined with the energy demands of the tumor may subsequently increase the patient's energy needs, leading to depletion of protein and fat stores in the face of anorexia and other factors that suppress oral intake.

Increased glucose utilization by both the host and the tumor results in increased lactate production. In the Cori cycle, glucose released by peripheral tissues is metabolized to lactate; in the liver, lactate is synthesized back to glucose. In patients with advanced cancer, an increased rate of the Cori cycle has been observed.[27] Gluconeogenesis from lactate is a very energy-inefficient process that requires an increased number of adenosine triphosphate (ATP) molecules to complete the cycle. Ultimately, this futile cycle increases energy needs further, thereby contributing to weight loss. Enhanced glucose consumption and elevated lactate levels are strongly negatively correlated with patient outcome.[28–30] Mitochondrial defects have also been reported to increase glycolysis.[31] Lastly, increases in glucose utilization are thought to be necessary for cancer progression.[31]

Similar to alterations in glucose metabolism, abnormalities in lipid metabolism are thought to contribute to weight loss in patients with cancer. Body fat is lost when lipolysis and fatty acid oxidation increase and lipogenesis decreases. In noncancer states, infusions of glucose generally suppress lipolysis; in some cancer patients, this process is diminished.[32] Furthermore, the reduction in lipogenesis is thought to reflect the influence of the cytokines. Lipid-mobilizing factor, which is produced by both the tumor and adipose tissue, induces lipolysis by promoting an increased in cyclic adenosine monophosphate production.[33] Of interest, lipid-mobilizing factor has been found in the serum of patients with CACS but not in healthy individuals. Levels of this factor have also been noted to parallel the degree of weight loss experienced.[33, 34] Other alterations in cellular metabolism related to lipid metabolism have also been reported, such as overexpression of the enzymes fatty acid synthase and choline kinase.

Tumor type and stage of disease also affect the nutritional status of cancer patients, with more advanced stages being associated with greater incidence of malnutrition. The heterogeneity of the population with CACS demonstrates that tumor phenotype and host response likely play key roles in the development of cachexia, as patients with similar cancer type and disease stage may vary significantly in terms of developing malnutrition. For example, patients with gastric, esophageal, head/neck, and pancreatic cancers develop malnutrition to a greater degree than do individuals with breast cancer and hematologic malignancies.[18] Patients with colon, prostate, lung and unfavorable non-Hodgkin's lymphoma often experience moderate weight loss (48–61%). Not surprisingly, people with advanced cancer experience the greatest degree of malnutrition.[35] Interestingly, weight gain following diagnosis and treatment has been associated with reduced survival in patients with breast cancer.[36]

Classification of cachexia as primary or secondary is important, as the treatment can differ depending on the type. The etiology of primary cachexia is not well understood and the condition is difficult to treat due the complex nature of CACS. By comparison, the causes of secondary cachexia (a functional inability to achieve an adequate intake) may be more amenable to treatment. Secondary cachexia often develops as a result of mechanical factors (e.g., obstruction) or related to the side effects of the various treatment modalities.

Although ameliorating the factors influencing the inability to consume adequate nutrition is critical for the prevention and treatment of malnutrition, curing the underlying cancer is the only intervention known to be successful in reversing true CACS. Pharmacologic management of cancer-associated symptoms may also be successfully employed to maintain or improve nutritional status (e.g., Megace, steroids). The bottom line is that the

preservation of nutritional status can prevent or at least delay the onset of CACS for many patients.

Oncological Treatment Modalities and Malnutrition

Oncological treatment modalities (e.g., chemotherapy, radiation, surgery) can have a profound impact on oral intake, leading to poor nutritional status and malnutrition (see Table 1.2).

Alterations in gastrointestinal absorptive area due to surgical procedures can induce malnutrition secondary to reductions in nutrient absorption or increased metabolic demands for postoperative healing concurrent with inadequate nutrition intake or nutrition support. Chemotherapy can produce a multitude of problems, including mucositis, taste changes, early satiety, diarrhea, constipation, anorexia, nausea, and emesis—all of which can have a profound impact on nutritional intake. Radiation therapy resulting in esophageal stricture, reflux, gastritis, radiation enteritis, xerostomia, dysphagia, odynophagia, diarrhea, and enteritis can also promote deteriorations in nutritional status. The presence of such treatment impact symptoms should be aggressively treated. Table 1.3

Table 1.2 ***Antineoplastic Therapies That May Impact Nutritional Status***

Treatment	***Potential Nutritional Impact***
Surgery	Increased nutrient needs for recovery and wound healing, malabsorption, early satiety, dehydration, abdominal cramping, diarrhea, bloating/gas, fluid/electrolyte imbalance, lactose intolerance, hyperglycemia
Chemotherapy	
Cytotoxic	Nausea, vomiting, anorexia, diarrhea, immunosuppression, fatigue, mucositis, peripheral neuropathy, dysgeusia, heightened sensitivity to tastes, metallic taste
Hormonal (glucocorticoids, anti-androgens/estrogens, gonadotropin-releasing hormone analog)	Hyperglycemia, edema, osteoporosis, nausea, vomiting, bone pain, hot flashes, hypercalcemia
Immunotherapy (interleukins, interferon alfa, monoclonal antibodies)	Anorexia, nausea, vomiting, diarrhea, fatigue, immunosuppression
Radiation	Thorax area: anorexia, dysphagia, esophagitis, heartburn, early satiety, fatigue Abdomen/pelvic area: nausea, vomiting, diarrhea, abdominal cramping/bloating/gas, lactose intolerance, malabsorption, chronic colitis and enteritis

Table 1.3 ***Nutritional Strategies for Management of Treatment-Related Symptoms***

Symptom	***Etiology***	***Recommendations***
Alterations in taste/smell, anorexia	Radiation, chemotherapy, cytokines, oncological therapy, pain, depression	Small, frequent, nutrient-dense meals; drinking fluids with meals; avoid low-calorie filler foods; increase physical activity; appetite stimulants
Constipation, diarrhea	Antineoplastic therapies	Low-fat, lactose-free diet; increase soluble fiber intake; avoid spicy foods; avoid caffeine; drink plenty of liquids; probiotics
Dysphagia	Tumor burden, antineoplastic therapies	Thickened, moist, soft or ground/pureed foods
Early satiety	Antineoplastic therapies	Small, frequent, nutrient-dense meals; avoid drinking fluids with meals
Fatigue	Tumor burden, antineoplastic therapies, anemia, dehydration, chronic pain, medications, stress, depression, poor nutrition	Small, frequent, nutrient-dense meals; physical activity; meal planning/assistance with shopping/meal preparation; manage stress and depression
Nausea/vomiting	Antineoplastic therapies	Small, frequent, low-fat, low-fiber meals; avoid spicy foods and caffeine; try not to eat 1–2 hours before treatment; antiemetics; hypnosis, acupuncture, music therapy also effective
Stomatitis, mucositis	Antineoplastic therapies	Soft, nonirritating foods; nutrient-dense liquids/nutritional supplements; Miracle Mouth/viscous lidocaine swishes; lemon/glycerine swabs
Weight loss	Tumor burden, cytokines, antineoplastic therapies	Small, frequent, nutrient-dense meals; try liquid/powder nutritional supplements; consume high-calorie, high-protein foods
Weight gain	Antineoplastic therapies, edema	Low-fat diet with lean meats; low-fat dairy products; whole grains, fruits, and vegetables
Xerostomia	Tumor burden, antineoplastic therapies	Drink/swallow small amounts of food at one time; sip water/fluid after each bite; try sweet or tart foods, soft/pureed foods; suck on hard candies; artificial saliva

outlines strategies that can be employed for managing treatment-related side effects that impact on nutritional intake.

Nutrition Intervention

Maintenance or improvement in nutrition status is the key goal of medical nutrition therapy for individuals undergoing treatment for cancer. Although many patients tolerate therapy well and experience few or no side effects, malnutrition is still a common entity that affects quality of life and survival for many persons with cancer. As previously described, many contributing factors have been implicated in promoting the deterioration in nutrition status. To maintain or improve nutritional status, all barriers associated with oral intake should be aggressively addressed unless aggressive intervention is not warranted.

Modifications in diet and eating habits may be necessary during treatment to reduce or eliminate the side effects of therapy. Weight maintenance is strongly recommended during therapy, with weight gain or loss being recommended based on the individual's nutritional status. Calorie and protein requirements may increase during treatment. Although there is no consensus regarding the optimal calorie and protein requirements for cancer patients, current guidelines recommend a caloric range of 25–35 kcal/kg/day and 1.0–1.5 g/kg/day protein for preserving or improving nutritional status.[37]

Given that many patients with cancer suffer severe alterations in nutritional intake, specialized nutrition support should be considered not only for improving and/or maintaining nutritional status, but also for improving quality of life. For patients undergoing blood or marrow transplantation, nutrition support—both enteral and parenteral—is life saving. For patients with cancer undergoing major surgical procedures, perioperative nutrition support appears beneficial for both adequately nourished and malnourished patients. Braga and colleagues[38] found that patients with cancer who had experienced a weight loss of more than 10% in the past 6 months and who consumed 1 liter/day of a diet enriched with arginine, omega-3 fatty acids (Ω-3), and nucleotides both preoperatively (for 5 days prior to surgery) and postoperatively (administered via jejunostomy) experienced fewer postoperative complications compared to the other study groups for whom perioperative nutrition was not provided.

In a separate study, Gianotti et al.[39] enrolled 305 well-nourished and malnourished patients scheduled to undergo resection of the stomach, pancreas, or colon. Patients were randomized to 1 of 3 groups: (1) consume 1 liter/day for 5 days preoperatively of the same immune-enriched diet as used in the Braga study; (2) receive the study diet preoperatively and postoperatively;

or (3) receive no nutrition support (this group received only IV fluids postoperatively until advancement to an oral diet). In comparison to the group receiving no nutrition support, the preoperative-diet-only group experienced a reduction in septic complications (30% versus 14%; $p = 0.009$) and length of stay (14.0 ± 7.7 days versus 11.6 ± 4.7 days). Complications and length of stay were also significantly reduced in the perioperative-diet group.

The authors from both studies note that the preoperative period may be an important time in which to modify the host response by using an immune-enhancing diet to maximally stimulate the immune system. In the Gianotti study,[39] BMI was also associated with outcomes, as patients with a BMI ranging from 18 to 25 experienced less morbidity; the risk for postoperative complications was found to increase as body weight increased.

Enteral or parenteral nutrition is often indicated for patients with cancer who are unable to consume adequate oral nutrition or in whom oral intake is contraindicated. Patients with head and neck cancers commonly require enteral nutrition via the percutaneous placement of a gastrostomy tube to prevent significant deteriorations in nutritional status during therapy and thereafter. Parenteral nutrition is also often indicated in patients with intestinal failure, which frequently results from severe malabsorption or malignant bowel obstructions. For patients with advanced cancers, however, the initiation of parenteral nutrition can be controversial. Home parenteral nutrition (HPN) support has been associated with long-term survival in select patients with advanced cancers with acceptable complication rates.[40, 41] Additionally, patients with a Karnofsky score greater than 50 reportedly experience an increase in survival when receiving HPN compared with patients scoring lower than 50.[42]

Hoda and colleagues recommend that HPN should be utilized only after an in-depth clinical assessment is completed on a patient-by-patient basis.[40] In general, nutrition support is not indicated for patients who are not expected to survive for more than three months. In many cases, patients must also meet the requirements established by insurance companies to obtain reimbursement for HPN expenses.

Dietary Supplements

Dietary supplements and complementary and alternative therapies are heavily advertised for cancer prevention and immune support. Many cancer survivors also take dietary supplements, more so than individuals without cancer.[43] Many oncological nutrition experts, however, recommend avoiding

dietary supplements, and particularly ingestion of pharmacologic levels of antioxidants, during treatment.

Similar to other disease states, whether benefits can be derived from post-treatment efforts to prevent cancer recurrence is unclear, although some studies have found an increase in morbidity and mortality with the use of some supplements.[44, 45] Additionally, the use of some herbal supplements has been associated with a reduction in the levels of chemotherapeutic agents in the body, which is of great concern given that patients hope to gain the maximal benefits related to treatment.[46, 47] Oral nutritional supplements, by contrast, can serve an important role in meeting nutritional needs in the face of adverse effects such as anorexia, early satiety, and fatigue associated with cancer. Deterioration of nutritional status not only plays a major role in the development of the cancer cachexia syndrome, but also leads to alterations in quality of life.[19, 48]

Concerns surrounding the influence of nutrition on tumor growth have long been voiced. For example, women with estrogen receptor-positive breast cancers often worry about consumption of soy protein, which is a rich source of isoflavones. The chemical structure of isoflavones is similar to that of estrogen, with isoflavones having the ability to bind to estrogen receptors. Under experimental conditions, isoflavones have been found to exert estrogen-like effects.[49] For this reason, they are commonly classified as selective estrogen-receptor modulators. Although the consumption of soy products has been linked with possibly reducing the risk for breast cancer, in some animal and in vitro studies, the soy isoflavone genistein has been observed to stimulate the growth of estrogen-sensitive tumors.[50–54] Thus, from a public health viewpoint, there is a critical need to discern whether the ingestion of soy products is safe for women with these types of tumors. To date, the results of neither animal nor clinical studies have allowed definitive conclusions to be made.

In a study investigating the influence of parenteral nutrition on tumor growth, Pacelli and colleagues recently reported that this type of nutrition did not stimulate tumor proliferation in malnourished patients with gastric cancer.[55] Conversely, when single nutrients have been studied, some have shown the ability to play a dual role in both cancer prevention and promotion. Folic acid is an example of one such nutrient: It may protect against cancer initiation, yet also promote the growth of preneoplastic cells. Some studies have shown that concentrations of serum folate levels are associated with a reduced risk for breast and colorectal cancer,[56, 57] particularly in individuals who consume alcohol.

Other studies have found an increased risk for prostate, breast, and ovarian cancers related to folic acid intake.[58–60] Notably, the rates of colorectal cancer incidence had been declining in the United States and Canada prior to the establishment of those countries' mandatory food folic acid fortification

programs.[61] Mason and colleagues[61] reviewed the data sets from the Surveillance, Epidemiology and End Result registry and Canadian Cancer Statistics and found that incidence rates began to reverse in parallel with the implementation of the food fortification programs in both countries. In their recent review of the literature, Smith et al.[62] concluded that the evidence is mounting suggesting that increasing folate levels in some people increases the risk for cancer. Clearly, further research is needed to determine the precise relationship between folic acid intake and the prevention and promotion of cancer.

SUMMARY

This chapter provided a brief discussion of many of the key elements that contribute to maintaining or improving the nutritional status of individuals with cancer. Cancer is not just a major cause of death—it is also becoming a chronic illness as more individuals are living with cancer longer, as they experience intermittent periods of active cancer with remission. The number of individuals who are cured of cancer is also increasing. Subsequent chapters of this book provide a more in-depth discussion of the nutrition care process and medical nutrition therapy for individuals with many of the different types of cancers as well as nutrition recommendations for cancer survivors.

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